

HC and LO Appendix - In-Silico Modeling of YCT-529

Capstone Project

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LO Appendix

LO: #CS-Computationaltools

Description of the LO from the course syllabus: Use appropriate computational tools (e.g., SymPy, Sage, Python packages, modeling software) to analyze or solve problems. This LO emphasizes tool selection, proper implementation, and the effective communication of results. Mastery entails using computational solutions to manage complexity, validate data, and present findings clearly and accurately.

What is a “4” level application of this LO as described in the course? A 4-level application involves correctly selecting and implementing computational tools while ensuring clear documentation, validation, and communication of results. This means integrating multiple tools to manage complexity, validating outputs, and effectively presenting findings. In pharmacokinetic modeling, this would involve configuring PK-Sim for simulations, using Python for data analysis, and ensuring consistency across outputs.

What would be a “4” level application of this LO in THIS project? A 4-level application in this project would involve simulating 16,000 individual pharmacokinetic profiles in PK-Sim, pre-processing large datasets in Python, and using advanced visualization techniques to compare inter-population variability, dietary effects, and drug-dose responses. Cross-validation of PK-Sim outputs with independent Python analyses would strengthen the computational framework.

Where is this LO applied in your project? This LO is applied throughout the project:

- **Methodology:** Details my use of PK-Sim for PBPK modeling and Python for statistical analysis.
- **Results:** Displays dose-response relationships, racial variability, and dietary condition effects.
- **Appendix C:** Documents how PK-Sim data was structured for Python analysis.
- **Appendix D:** Explains my coding workflow and key computational methods.

How have I applied this LO in THIS project? Evaluate the strength of my application: **Application 1: Multi-Platform Computational Workflow**

I integrated PBPK modeling (PK-Sim), large-scale data processing (Python), and statistical visualization to analyze YCT-529's pharmacokinetics. PK-Sim's built-in tools were insufficient for cross-cohort dose-response analysis, necessitating external computation and validation.

Application 2: Large-Scale Data Pre-Processing

With 16,000 individual simulations, I wrote Python scripts to aggregate, restructure, and convert units for downstream analysis. PK-Sim could not directly compare population-based trends, requiring me to algorithmically compute C_{\max} distributions, dose-normalized plasma concentrations, and inter-population variability.

Application 3: Validation and Advanced Visualization

I ensured computational reproducibility by cross-validating PK-Sim results with Python-generated statistical summaries. Additionally, I developed custom visualization techniques (dose-stratified C_{\max} plots, overlay comparisons for placebo-drug response, and dietary condition sensitivity analyses) that PK-Sim's built-in graphing tools could not generate.

Consideration for a 5: Novel Application Beyond the Course Scope A 5-level application extends beyond standard coursework expectations by demonstrating innovation, computational complexity, and interdisciplinary expertise. This project surpasses typical applications in three ways:

1. **Interdisciplinary Integration:** I established a workflow combining PBPK modeling, statistical analysis, and custom visualization, akin to professional pharmacometric research.
2. **Independent Model Refinement:** Unlike typical coursework, my Python pipeline allowed me to handle 16,000 simulations algorithmically, enabling insights beyond PK-Sim's built-in functionality.
3. **Beyond-Syllabus Computational Strategy:** Most applications focus on a single-tool approach. My hybrid strategy—PBPK modeling, data engineering, validation, and visualization—reflects industry-grade pharmacokinetic workflows.

By designing a multi-tiered computational pipeline that enhances PBPK modeling and data analysis, this application qualifies as a 5-level demonstration of #CS-Computationaltools.

LO: #CS110-PythonProgramming

Description of the LO from the course syllabus: Writes Python programs to implement, analyze, and compare algorithms and apply data structures. When appropriate, produce Python code to plot and visualize meaningful performance metrics.

What is a “4” level application of this LO as described in the course? A 4-level application demonstrates correct implementation of required functionality, strategic test case design, and thorough validation. It also includes simulations and Python-based visualizations to analyze and compare algorithmic performance. A strong application would show correctness through explicit test cases and leverage Python’s scientific computing libraries to generate insightful visualizations.

What would be a “4” level application of this LO in THIS project? A 4-level application in this project would involve writing Python programs that process, analyze, and visualize large-scale pharmacokinetic data, ensuring the correct implementation of statistical transformations, dose-response relationships, and inter-population comparisons. Additionally, it would include well-structured test cases verifying data integrity, accuracy, and reproducibility.

Where is this LO applied in your project? This LO is applied in:

- Appendix D: Contains Python scripts used for pharmacokinetic modeling and data visualization.
- Methods: Discusses Python’s role in pre-processing and statistical validation.
- Results: Includes dose-stratified C_{\max} plots, placebo-drug response comparisons, and dietary sensitivity analyses.

How have I applied this LO in THIS project? Evaluate the strength of my application: **Application 1: Algorithmic Data Processing**

I wrote Python scripts to aggregate, restructure, and normalize 16,000 pharmacokinetic simulations. This required applying vectorized NumPy operations and pandas transformations to efficiently handle large datasets while preserving dose-response relationships.

Application 2: Validation with Test Cases

To ensure correctness, I implemented test cases that cross-validated PK-Sim outputs with

Python-generated results, ensuring no discrepancies in pharmacokinetic parameters like C_{\max} , T_{\max} , and clearance rates.

Application 3: Visualization of Pharmacokinetic Trends

I used Matplotlib and Seaborn to create custom visualization techniques, including dose-normalized C_{\max} distributions, stratified plasma concentration curves, and placebo-drug response overlays, providing analytical insights beyond PK-Sim's built-in tools.

The way I developed an automated computational pipeline for pharmacokinetic analysis makes my application a 4-level standard for #CS110-PythonProgramming.

LO: #NS164-ResearchMethods

Description of the LO from the course syllabus: Conduct scientific research; analyze experimental protocols and results. This LO focuses on designing and executing scientific experiments, analyzing protocols, and interpreting results with rigor, precision, and critical evaluation. It involves following established methodologies, systematically collecting data, and assessing the validity and reliability of both the approach and the outcomes.

What is a “4” level application of this LO as described in the course? A 4-level application of this LO demands more than just correctly executing experimental protocols—it requires rigorous justification of each methodological choice. A strong application critically evaluates the strengths and limitations of different approaches, ensuring that the study design is not just functionally correct but also scientifically sound. For instance, in my previous coursework, I achieved a 4-level application by assessing competing methodologies in molecular biology experiments, discussing how their differences affected data reliability. Similarly, in this project, achieving a high-level application requires going beyond just running pharmacokinetic simulations—I must demonstrate why each model choice, parameterization, and validation step was the most appropriate.

Where is this LO applied in my project? My application of this LO is deeply embedded in my methodology, data validation, and comparative analysis - extended to Appendix C. From the outset, I carefully justified why PK-Sim was the best platform for YCT-529 pharmacokinetics, comparing it against alternative modeling tools like Bio-Gears. Beyond just citing its features, I explained how its whole-body physiologically based pharmacokinetic (PBPK) framework was better suited for capturing systemic drug interactions than compartmental models.

But research methodology is more than just picking the right tools—it’s also about ensuring that those tools produce reliable, reproducible, and interpretable data. That’s why I didn’t stop at running PK-Sim simulations. To validate my model, I cross-checked its plasma concentration-time profiles using Python-based statistical analysis, confirming consistency across different simulation outputs. I even compared my results with Atazanavir, a drug with a well-documented pharmacokinetic profile, to ensure my modeling choices produced realistic estimates.

Another major application of this LO was in how I structured my dataset for analysis. PK-Sim’s raw output wasn’t in a form that allowed for easy cross-cohort comparison, so I developed a data pre-processing pipeline to restructure simulation results into an aggregated format. This allowed me to examine dose-dependent trends, inter-population differences, and key pharmacokinetic parameters like C_{\max} and clearance rates in a way that the original software couldn’t directly visualize.

What takes this beyond a 4 and into a 5? A typical application of this LO would stop at well-justified modeling and validation. However, my work extends beyond standard expectations in three key ways:

1. **Mechanistic Exploration:** Rather than treating drug elimination as a simple first-order process, I investigated whether enterohepatic recirculation contributed to YCT-529’s 40 $\mu\text{g/L}$ plateau beyond hour 10. Identifying this as a potential explanation required integrating pharmacokinetic modeling with mechanistic hypotheses—an approach not typically expected in coursework.

2. **Application to Dose Optimization:** Instead of merely analyzing pharmacokinetics, I connected my findings to practical dose adjustments. By proposing race-specific dosing strategies, I translated raw computational results into actionable insights that could inform clinical decision-making. This level of applied pharmacokinetic analysis is more aligned with industry research than standard undergraduate coursework.

3. **Multi-Platform Validation:** Most pharmacokinetic modeling studies rely on a single platform. I enhanced methodological robustness by validating PK-Sim’s results using a Python-based secondary analysis and cross-referencing trends against reference drug models. This step ensured that my conclusions were not just internally consistent but also externally validated.

Final Reflection This project wasn’t just about running simulations—it was about designing, validating, and critically analyzing a pharmacokinetic model to derive meaningful conclusions. By integrating mechanistic hypotheses, practical dose optimization, and cross-platform validation, my research surpasses standard coursework expectations.

Given the depth, complexity, and novel application of my approach, this work qualifies as a 5-level demonstration of #NS164-ResearchMethods.

LO: #ns164-modelselection

Description of the LO from the course syllabus: Evaluate the appropriate clinical and pre-clinical model for testing therapeutic applications. This LO requires selecting a model type—in vitro, in vivo, in silico, or ex vivo—and providing a well-reasoned justification. A strong application involves not only identifying an appropriate model but also discussing the trade-offs of different approaches. A 5-level application extends beyond conventional comparisons, offering a novel perspective or methodology in model selection.

What is a “4” level application of this LO as described in the course? A 4-level application requires correctly identifying the relevant model type, explaining its suitability, and comparing alternative models with a detailed discussion of their strengths and weaknesses. For instance, selecting an in silico PBPK model over in vitro hepatocyte assays based on systemic applicability would meet this standard. A thorough justification of why one approach was superior—supported by literature, known pharmacokinetic properties, and experimental feasibility—would strengthen the application.

What makes this a “5” level application in THIS project? A 5-level application needed to go beyond selecting PK-Sim as the best in silico tool. I framed my approach as a hybrid validation pipeline, integrating computational pharmacokinetics with independent Python-based data processing. Instead of relying solely on PK-Sim’s built-in tools, I cross-validated simulated outputs, ensuring internal consistency across multiple computational platforms. Additionally, I leveraged a simulated placebo arm (MCC) within a PBPK framework, an unconventional but effective way to assess YCT-529-specific pharmacokinetics.

Where is this LO applied in this project? This LO is central to my Methodology, particularly the sections on model selection and validation strategy. I justified my choice of PK-Sim over other pharmacokinetic simulators like GastroPlus or BioGears, showing how each tool differs in enzyme modeling, transporter integration, and physiological scaling. It also appears in the Limitations, where I acknowledge the trade-offs of PBPK modeling and propose experimental validation pathways.

How have I applied this LO in THIS project? Evaluate the strength of my application: Application 1: Strategic Model Selection

Selecting a PBPK model over conventional in vitro or in vivo studies required careful consideration. In vivo pharmacokinetic profiling would have provided empirical data but was impractical due to ethical and logistical constraints. While in vitro enzyme kinetics assays could estimate metabolism rates, they lacked systemic relevance. I chose an in silico PBPK framework, which allowed me to simulate YCT-529's absorption, metabolism, and elimination across diverse populations while incorporating key physiological parameters.

Application 2: Multi-Tiered Computational Validation

Rather than solely relying on PK-Sim, I conducted a Python-based validation to verify model reliability. By reanalyzing dose-stratified C_{\max} trends, placebo-drug response comparisons, and inter-population variability, I ensured my conclusions were not dependent on a single computational environment. This multi-tiered verification reinforced the robustness of my results.

Application 3: Novel Use of a Simulated Placebo Control

Most PBPK studies do not incorporate placebo pharmacokinetics, yet I simulated MCC as an inert control to establish a baseline for systemic retention. This approach eliminated confounding factors, allowing me to isolate true drug absorption effects. By integrating a placebo arm within an in silico model, I extended my methodological design beyond conventional pharmacokinetic workflows.

Consideration for a 5: Novel Application Beyond the Course Scope This project surpasses standard coursework expectations in three critical ways:

- **Cross-Validation Across Platforms:** I did not just rely on PBPK simulations; I implemented a secondary analytical framework to validate predictions.
- **Interdisciplinary Model Design:** Instead of focusing solely on pharmacokinetics, I integrated data engineering and validation techniques, mimicking real-world pharmacometric research.
- **Innovative Model Implementation:** By embedding a placebo arm within a computational framework, I demonstrated a methodological advance in in silico pharmacokinetics.

By designing a hybrid PBPK validation strategy that enhances computational pharmacokinetics, this application qualifies as a 5-level demonstration of #ns164-modelselection.

HC Appendix

HC: #thesis

Description of the HC from the course syllabus: Formulate a well-defined thesis. A strong thesis serves as the central guiding argument for any research project, ensuring clarity, coherence, and logical progression. A well-crafted thesis is concise, arguable, substantial, precise, sets up forthcoming evidence, and relevant (CASPER). Mastery of this HC requires the ability to construct a thesis that effectively frames the research, integrates supporting claims, and evolves based on findings.

Previous Challenges and Improvements: In an earlier draft, I received feedback indicating that my thesis statement was overly prominent within the paper’s structure, disrupting the natural flow of my argument. The critique pointed out that while my thesis was strong, its placement in the introduction did not align with academic conventions. After discussing this with my professor, I made a strategic decision to relocate the thesis to the Appendix. This adjustment allowed me to retain the clarity of my central argument without compromising the professional structure of my paper.

How I Applied This HC in My Project: Application 1: Developing a Precise, Arguable, and Evidence-Based Thesis

I ensured that my thesis clearly articulated the central claim of my research: Computational pharmacokinetics provides an effective and scalable approach to optimizing YCT-529’s dosing across diverse populations. This claim is precise, as it defines the scope of my work; arguable, as it presents a stance that can be tested against alternative approaches; and evidence-based, as I validate it through simulations and comparative pharmacokinetic analysis.

Application 2: Structuring the Thesis to Guide the Research

Throughout the project, my thesis evolved to align with emerging findings. Initially, I hypothesized that population-level variability would necessitate minor dosing adjustments, but as the research progressed, I found significant inter-population differences in drug metabolism. This led to a refined thesis that emphasizes tailored pharmacokinetic modeling for personalized dosing. This iterative refinement demonstrates a deep engagement with the research process and ensures that the thesis remains aligned with the actual results.

Application 3: Integrating the Thesis Without Disrupting Paper Structure

Rather than forcing the thesis into the introduction, I strategically moved it to the Appendix, allowing the introduction to flow naturally into the research background. This

decision maintained academic integrity while still ensuring that my thesis was explicitly defined. This approach demonstrates an understanding of formal research structures and a flexible application of academic writing conventions.

Evaluation of My Application: By developing a concise yet substantial thesis, refining it based on findings, and strategically placing it in a manner that enhances readability, I have applied this HC at a 4-level proficiency. However, the adaptability in structure, combined with the methodological rigor in refining my claim, suggests a creative and effective approach that aligns with a 5-level application.

HC: #interventionalstudy

Description of the HC from the course syllabus: Design and interpret experimental studies. A true experiment involves independent variables that are manipulated, dependent variables that are measured, and the control of extraneous factors to establish causal relationships. Unlike observational studies, interventional studies actively introduce treatments or modifications to examine their effects.

What is a “4” level application of this HC as described in the course? A 4-level application involves designing a rigorous, well-controlled experimental study where variables are explicitly justified, confounding factors are accounted for, and the results allow for strong causal inferences. This includes clear experimental design, appropriate control groups, and a discussion of extraneous influences. Additionally, study limitations and potential refinements should be identified.

What would be a “5” level application of this HC in THIS project? A 5-level application extends beyond traditional experimental design by using novel methodologies or framing interventional studies in a unique way. In this project, I simulate an interventional study through PBPK modeling, where YCT-529 is “administered” computationally across 16,000 simulated individuals at different doses and under varying conditions. This differs from traditional wet-lab experiments but still tests hypotheses, controls variables, and evaluates outcomes, making it a high-level intervention.

Additionally, I compare YCT-529 pharmacokinetics to validated clinical data for Atazanavir, treating Atazanavir as a benchmark control for evaluating model accuracy. This cross-validation approach ensures real-world relevance of computational interventions, a rarely explored extension of interventional study design.

Where is this HC applied in your project? This HC is primarily applied in the Methodology section, where I detail my computational intervention approach via PBPK modeling. It also appears in the Discussion, where I critically analyze the intervention outcomes against real-world pharmacokinetic data.

How have I applied this HC in this project? Evaluate the depth of application:
Application 1: Computational Drug Intervention via PBPK Modeling

I designed an in silico interventional study where YCT-529 was tested at different doses and across demographic groups using PK-Sim. Unlike a static dataset analysis, this approach actively manipulates variables (dose, population, diet conditions) to observe pharmacokinetic responses, akin to a clinical intervention but without human subjects.

Application 2: Benchmarking Against Clinical Data for Atazanavir

To assess intervention validity, I compared YCT-529 pharmacokinetics to Atazanavir, a drug with established CYP3A4 metabolism. This serves as a positive control, ensuring my simulated interventions align with known pharmacokinetic behaviors.

Application 3: Race-Specific Dose Optimization as an Experimental Outcome

Beyond simply testing a drug intervention, I used results to propose race-specific dose modifications, similar to precision medicine approaches for drugs like tacrolimus and warfarin. This extends interventional study design beyond a single-variable analysis to a multi-factorial dose-response investigation.

Consideration for a 5: This project redefines the scope of an interventional study by demonstrating that computational interventions can serve as preliminary trials before human testing. The integration of PBPK modeling, benchmark comparisons, and race-specific interventions represents a novel, creative extension of traditional interventional study design, justifying a 5-level application.

HC: #studyreplication

Description of the HC from the course syllabus: Evaluate and incorporate replicability in empirical study designs. Study replication ensures the validity of scientific findings by reproducing experimental results under similar or varied conditions. It strengthens confidence in conclusions by assessing whether observed effects persist across different methods, populations, or analytical approaches.

What is a “4” level application of this HC as described in the course? A 4-level application demonstrates a deep understanding of study replication by designing or

executing a replication study to validate results. This includes identifying sources of variability, ensuring consistency in experimental methods, and critically assessing whether the replicated findings confirm or challenge the original study. The application is well-justified, technically precise, and free from methodological gaps. A strong example would be reanalyzing an existing dataset using independent statistical methods or recreating a pharmacokinetic model to verify its predictive accuracy.

What would be a “4” level application of this HC in THIS project? In this project, a 4-level application involves replicating Atazanavir pharmacokinetics within my PK-Sim model to validate the accuracy of my computational framework. By lifting Atazanavir’s compound properties and designing an independent simulation protocol, I was able to test whether my modeled enzymatic and clearance pathways produced results consistent with clinical data. A successful replication indicated that my metabolic assumptions, population scaling, and enzymatic kinetics were properly parameterized, thereby increasing confidence in the model’s ability to predict YCT-529 pharmacokinetics.

Where is this HC applied in your project? This HC is primarily applied in the Methods and Validation sections, where I describe my approach to simulating Atazanavir as a benchmark compound. The replication process played a critical role in confirming that the systemic clearance, C_{\max} , and elimination kinetics in my PBPK model were physiologically realistic. Additionally, this HC is reflected in the Results section, where I compare the Atazanavir simulation outcomes against clinical data to demonstrate model validity.

How have I applied this HC in this project? One of the core challenges in PBPK modeling is ensuring that simulated drug behavior aligns with known, real-world pharmacokinetics. I applied study replication by independently running an Atazanavir simulation, comparing my results to published clinical data. The close alignment between my simulated and observed concentration-time profiles confirmed that my model accurately captured CYP3A4 metabolism, biliary excretion, and systemic drug clearance.

Additionally, this replication served as an internal consistency check. If Atazanavir—a drug with well-characterized PK parameters—had yielded unrealistic simulation results, it would have flagged potential errors in my model’s enzyme kinetics or clearance rates. By verifying that Atazanavir behaved as expected, I demonstrated a rigorous approach to validating my model before applying it to YCT-529 predictions.

Lastly, my study replication allowed me to fine-tune my PK-Sim parameterization strategies. For example, observing Atazanavir’s clearance patterns informed my popula-

tion variability assumptions, which were then applied to refining YCT-529 simulations. This illustrates how replicating existing pharmacokinetic models enhances confidence in novel predictions, a critical component of computational pharmacology and translational drug development.

HC: #significance

Description of the HC from the course syllabus: Apply, interpret, and distinguish practical and statistical significance. This involves understanding the difference between observing a pattern that is likely not due to chance (statistical significance) and evaluating whether that pattern is large enough to matter in practice (practical significance).

What is a “4” level application of this HC as described in the course? A “4” level application demonstrates deep understanding by conducting and interpreting both statistical and practical significance tests, using appropriate quantitative tools like p-values and effect sizes (e.g., Cohen’s d). It carefully distinguishes these concepts, explains their implications for real-world applications, and avoids common pitfalls such as overinterpreting statistical significance in the absence of practical importance. Strong applications also justify the choice of significance level and effect size metric, incorporate Type I/II error considerations, and communicate findings clearly.

What would be a “4” level application of this HC in THIS project? In this project, a “4” level application would involve statistically comparing pharmacokinetic parameters (e.g., C_{\max}) across experimental conditions (e.g., dietary states), reporting both p-values and effect sizes (Cohen’s d), and interpreting these in terms of both statistical and real-world relevance. It would require distinguishing when a significant p-value reflects a meaningful drug absorption difference and when it may be practically irrelevant. It also includes explicitly explaining what Cohen’s d means in the pharmacokinetic context and how the observed percentage differences connect to the practical significance of YCT-529’s absorption profiles.

Where is this HC applied in your project? This HC is primarily applied in the **Results** and **Discussion** sections. In the Results, I conducted a one-way ANOVA ($F = 793.45$, $p < 0.001$) comparing YCT-529 C_{\max} values across three dietary conditions and followed it with post-hoc Tukey’s HSD tests. I reported Cohen’s d values of 1.38 and 1.61, indicating large effect sizes between fasted vs. light meal and fasted vs. high-fat breakfast, respectively. I also contextualized these values with percentage

differences (50.0% and 61.9%) to connect statistical differences to meaningful real-world implications. In the Discussion, I interpreted these findings to make a dosing recommendation: YCT-529 should be administered in a fasted state to maximize absorption.

How have I applied this HC in this project? I applied #significance by not only showing that differences in C_{\max} across dietary conditions were statistically significant (e.g., $p < 0.001$), but also interpreting how large those differences were in practical terms using Cohen’s d . For example, a $d = 1.61$ between fasted and high-fat conditions indicated a very large and meaningful difference, one that could affect clinical dosing decisions. I explained what Cohen’s d tells us—namely, how large a difference is relative to variability—and emphasized that a p -value alone is not enough to determine if a difference matters in practice. I also added this explanatory sentence to make my interpretation transparent: *“Cohen’s d indicates practical significance by showing how large the difference between two groups is, relative to the variability. While a p -value tells us if an effect likely exists (statistical significance), Cohen’s d tells us how meaningful or impactful that effect is in real-world terms.”* This helped frame my statistical analysis as both analytically rigorous and clinically actionable. Additionally, I avoided common pitfalls by interpreting small effect sizes (e.g., $d = 0.22$ for light vs. high-fat meals) as negligible, despite non-significant p -values, and by using Tukey’s HSD rather than multiple t -tests to control for family-wise error.

HC: #evidencebased

Description of the HC from the course syllabus: Identify and appropriately structure the information needed to support an argument effectively. This HC requires selecting compelling, well-cited evidence that aligns with the argument, structuring it for clarity, and addressing counterarguments or contradictions to reinforce credibility.

What is a “4” level application of this HC as described in the course? A 4-level application entails not only presenting well-supported arguments but also structuring evidence logically, addressing potential counterarguments, and ensuring every claim is backed by substantial, high-quality evidence. This includes carefully choosing between qualitative and quantitative evidence, using data visualizations where appropriate, and ensuring that the presented evidence strengthens the argument.

What would be a “4” level application of this HC in THIS project? In this project, a 4-level application involves integrating pharmacokinetic data, enzymatic

metabolism pathways, and comparative drug studies to support claims regarding YCT-529's absorption, distribution, metabolism, and elimination. This means using clinical data from Atazanavir simulations as a benchmark, referencing PBPK modeling literature, and aligning computational findings with known metabolic principles. Additionally, figures such as plasma concentration-time profiles serve as direct evidence to illustrate trends in systemic exposure.

Where is this HC applied in your project? This HC is most evident in the Results and Discussion sections, where I analyze plasma concentration trends and enzymatic interactions. It is also applied in the Methodology section, where I justify parameter selection using literature-backed evidence. Throughout the paper, Vancouver-style citations ensure proper attribution and alignment with scientific publishing norms.

How have I applied this HC in this project? One key application of this HC is in validating my PBPK model. To ensure reliability, I simulated Atazanavir pharmacokinetics independently, then compared the results to published clinical data. The strong alignment between simulated and real-world data provided compelling evidence that my enzymatic and clearance parameters were well-calibrated.

Another critical application is structuring comparative evidence to justify race-specific dosing strategies. By analyzing how YCT-529's C_{\max} varied across populations, I argued that East Asians require lower doses due to reduced CYP3A4 activity, while Black Americans may need higher doses. This claim was substantiated using literature on racial pharmacokinetic variability in tacrolimus and warfarin.

Lastly, I applied evidence-based reasoning in dietary condition analysis, demonstrating how food intake affects systemic exposure. Fasting led to higher C_{\max} , a pattern supported by studies on bile-mediated drug solubilization. These examples illustrate a well-structured, data-driven approach, making this a strong application of #evidence-based.

HC: #professionalism

Description of the HC from the course syllabus: Follow established guidelines to present yourself and your work products professionally. This HC emphasizes adherence to field-specific norms, ensuring clarity, accuracy, and credibility in communication.

What would be a “4” level application of this HC in THIS project? A 4-level application requires strict adherence to professional formatting standards, including

proper citation styles, structured documentation, and clear, reproducible presentation of research.

How is this HC applied in my project? I demonstrated professionalism by using Vancouver citation style, the standard in pharmacokinetics, ensuring my work aligns with scientific conventions. My GitHub repository includes structured documentation, dataset access instructions, and clear computational methodology, reinforcing transparency and reproducibility.

I formatted pharmacokinetic tables with consistent units, clear headings, and readable columns. Additionally, I refined figures and graphs to ensure clarity and accuracy. Consulting my professor, I moved my thesis statement to the appendix, preserving the research structure while maintaining clarity.

By rigorously maintaining professional standards in writing, citation, and data presentation, I demonstrate a strong 4-level application of professionalism.